Message

From: eu-toxrisk-sab-request@eurtd.com [eu-toxrisk-sab-request@eurtd.com]
on behalf of Thomas Steger-Hartmann [thomas.steger-hartmann@bayer.com]
Sent: 7/27/2016 6:58:01 AM
To: KNIGHT Derek [Derek.KNIGHT@echa.europa.eu]
CC: VIRTA Tarja [Tarja.VIRTA@echa.europa.eu]; eu-toxrisk-sab@eurtd.com; Benjamin Barton (barton@arttic.eu) [barton@arttic.eu]; Water, B. van de (water_b@lacdr.leidenuniv.nl) [water_b@lacdr.leidenuniv.nl]
Subject: [eu-toxrisk-sab] RE: EUTox Risk - SAB follow up to meeting at General Assembly & input for teleconference next week
Attachments: draft letter from SAB to EFSA for support for EUToxRisk DJK July 2016_TSH.docx

Dear Derek

Thanks for drafting this – very convincing.

I have only three minor comments/changes, one particularly pertaining to a potential travel to EFSA: I won't be able to go there, but I'd be happy to see you driving this process, i.e. if you can travel to Parma, please do so!

WRT a letter to EMA: I will ask Jan Willem, whether he will take charge or whether we should revise your draft that it also fits to EMA.

Kind regards

Thomas

Bayer: Science For a Better Life

Pharmaceuticals Division
Bayer Pharma AG
Investigational Toxicology
Berlin: Müllerstraße 178, S116-5-523
D-13352 Berlin, Germany
Phone: +49 30 468 14256
WUP: Aprather Weg 18a, 514-3-301
D-42113 Wuppertal
Phone: +49 202 36 4997
Mobile: +49 1703326034
Fax: +49 30 468 18172
E-mail: thomas.steger-hartmann@bayer.com
Web: http://www.pharma.bayer.com

Vorstand: Dieter Weinand, Vorsitzender | Christoph Bertram
Vorsitzender des Aufsichtsrats: Hartmut Klusik
Sitz der Gesellschaft: Berlin | Amtsgericht Charlottenburg, HRB 283 B

From: eu-toxrisk-sab-request@eurtd.com [mailto:eu-toxrisk-sab-request@eurtd.com] **On Behalf Of** KNIGHT Derek
Sent: Dienstag, 26. Juli 2016 17:32
To: Thomas Steger-Hartmann
Cc: VIRTA Tarja; eu-toxrisk-sab@eurtd.com; Benjamin Barton (barton@arttic.eu); Water, B. van de (water_b@lacdr.leidenuniv.nl)
Subject: [eu-toxrisk-sab] EUTox Risk - SAB follow up to meeting at General Assembly & input for teleconference next week

Dear Thomas,

I attach a suggested text for a letter from the SAB to EFSA requesting support for EU-ToxRisk. As you see I have suggested 3 specific means of co-operation, but I will let the SAB decide if these are OK or if we want to change or add to them. I have included the contact details in the letter so you can send a signed copy of the letter by e-mail (I suggest you send a letter not an e-mail message).

I am not sure if you also wanted me to draft a letter to EMA or if Jan is doing this. If you want me to do this, I will prepare one as an 'edited down' version of the letter to EFSA.

Best wishes from,

Dr Derek J Knight
Senior Scientific Advisor
Executive Director's Office
European Chemicals Agency
Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland
Tel. + 358 9 6861 8215
derek.knight@echa.europa.eu
echa.europa.eu

From: eu-toxrisk-sab-request@eurtd.com [mailto:eu-toxrisk-sab-request@eurtd.com] **On Behalf Of** Thomas Steger-Hartmann
Sent: 02 July 2016 18:45
To: KNIGHT Derek <Derek.KNIGHT@echa.europa.eu>; eu-toxrisk-sab@eurtd.com; Benjamin Barton (barton@arttic.eu) <barton@arttic.eu>
Cc: VIRTA Tarja <Tarja.VIRTA@echa.europa.eu>
Subject: [eu-toxrisk-sab] RE: EUTox Risk - SAB follow up to meeting at General Assembly & input for teleconference next week

Dear Derek

We wil discuss your PK proposal next Thursday at the SAB TC.

WRT letter to EFSA & EMA, I agree, we should also alert them in parallel to EUTOXRisk's Steering Committee. Would it be possible for you, DEREK to come up with a draft letter? I'd be happy to finalize it together with you and sign it on behalf of the SAB.

Kind regards

Thomas

Bayer: Science For a Better Life

Pharmaceuticals Division
Bayer Pharma AG
Investigational Toxicology
Berlin: Müllerstraße 178, S116-5-523

D-13352 Berlin, Germany
Phone: +49 30 468 14256
WUP: Aprather Weg 18a, 514-3-301
D-42113 Wuppertal
Phone: +49 202 36 4997
Mobile: +49 1703326034
Fax: +49 30 468 18172
E-mail: thomas.steger-hartmann@bayer.com
Web: http://www.pharma.bayer.com

Vorstand: Dieter Weinand, Vorsitzender | Christoph Bertram
Vorsitzender des Aufsichtsrats: Hartmut Klusik
Sitz der Gesellschaft: Berlin | Amtsgericht Charlottenburg, HRB 283 B

From: KNIGHT Derek [mailto:Derek.KNIGHT@echa.europa.eu]
Sent: Freitag, 1. Juli 2016 14:36
To: Thomas Steger-Hartmann; eu-toxrisk-sab@eurtd.com; Benjamin Barton (barton@arttic.eu)
Cc: VIRTA Tarja
Subject: EUTox Risk - SAB follow up to meeting at General Assembly & input for teleconference next week

Dear SAB,

I cannot attend the TC next week, but this is a follow-up to the short SAB meeting today:

Regarding engagement of regulators with EU-ToxRisk:

- I have asked the chair of ECHA's Member State Committee (MSC) to seek volunteers from the MS competent authorities to help with EU-ToxRisk. I have suggested the main work would be to have input into the regulatory relevance of case studies & in particular to give a view on any 'mock submissions'. I will keep you up to date.
- I think that the SAB should send an e-mail to both EFSA & EMA to ask for their support, not just let EU-ToxRisk members contact them without warning them! Do you want me to do this? Or Thomas as chair could do this. Please confirm.

My AOB item was to ask the SAB to devise a text for me to send to Dr Christian Desaintes of DG R&I who has sought input on possible EU-funded research on toxickinetics targeted to support read-across justifications for REACH/CLP. This is the background information with my initial thoughts. I have informed Christian that the SAB will help in the further input has asked for. Clearly any research in this area would be of benefit to EU-ToxRisk as it is complementary. At the SAB TC can you arrange for the text of the 'Scope' section to be completed? Then I will send it to Christian. I have had input from within ECHA on the 'title', 'specific challenge' & 'expected impact', but the SAB is welcome to comment to improve these sections if appropriate.

I think we could (loosely) follow the format used by R&I for research Calls, at least to address the key aspects. A good example is that for PHC-33-2015 that was https://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/topics/697-phc-33-2015.html . This means covering:

Topic (i.e .the name), e.g. 'Toxicokinetic prediction tools to enhance the confidence of reading across the toxicological properties between chemical substances to improve predictive human safety testing'

The following aspects of **Topic description**:

Specific challenge, e.g.

'A barrier to the successful use of read-across in regulatory toxicology, such as for the REACH & CLP Regulations, is establishing that the toxicokinetic (TK) behaviour of the 'source' & 'target' substance(s) are sufficiently similar that the validity of reading across the toxicology results of the tested 'source' substance

to the untested 'target' substance is not compromised. TK covers Absorption (including the rate), Distribution, Metabolism & Excretion; hence this is commonly referred to as ADME. The key question to address is whether (minor) differences in chemical structure between the 'source' & 'target' substances in the read-across case will affect the TK behaviour significantly, i.e. to an extent that will invalidate the read-across justification. Although there are *in silico* & *in vitro* methodologies for predicting TK properties (including rate of absorption), these are not necessarily reliable in distinguishing between closely-related structures (as in read-across cases).'

Scope, i.e. take inspiration from the text of the PHC-33-2015 Call, e.g.

'Proposals should capitalise on advances in all relevant fields of science to understand .....with the objectives of developing and validating routine, non-animal approaches for ..... The research may include the development of .....
Proposals should involve, amongst others, research communities, SMEs, industry and regulatory agencies as appropriate. Proposals should demonstrate efficient mechanisms for the co-ordination of activities and exchange of information, and should include a timeline for delivery of test methods.
In line with the Union's strategy for international cooperation[1] in research and innovation, cooperation is encouraged with similar initiatives in the USA and elsewhere, and would be highly beneficial from scientific and economic standpoints'

Somewhere, perhaps in this 'scope' section, you could state that you anticipate a toolkit &/or guidance for use in address the TK issue in read-across justifications (perhaps mention the RAAF & the TK AEs?) covering a wide range of types of chemical substance (in terms of chemical structure, PC properties & toxicological properties) or the scope of the tools/methodologies (in terms of structure etc.).

Also do you have specific suggestions how to go about the research? You suggested using new subacute rat toxicity studies to measure TK. What about other ideas? E.g. collecting existing TK prediction techniques (*in silico & in vitro*) & 'road testing' them in read-across cases (validated against animal TK results) & investigating the suitability of these techniques to distinguish differences resulting from minor differences in chemical structure. Other ideas?

Expected impact, i.e. again adapt the text from the PHC-2015 Call, e.g.:

- Improved toxicological knowledge to encourage 'read across' between chemical substances for use in different research and regulatory domains.
- Advancement of international co-operation in the field of predictive toxicology and human safety testing.
- Reduced use of laboratory animals in safety testing

Dr Derek J Knight
Senior Scientific Advisor
Executive Director's Office
European Chemicals Agency
Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland
Tel. + 358 9 6861 8215
derek.knight@echa.europa.eu
echa.europa.eu

From: eu-toxrisk-sab-request@eurtd.com [mailto:eu-toxrisk-sab-request@eurtd.com] **On Behalf Of** Thomas Steger-Hartmann

Sent: 27 June 2016 09:23
To: eu-toxrisk-sab@eurtd.com
Subject: [eu-toxrisk-sab] EUTox Risk - SAB presentation

Dear colleagues

Thank you all for your valuable feedback. I have tried to incorporate all aspects.

I'll participate Thursday and Friday (arriving late Wednesday evening).

We will certainly include other topics on the fly as they are identified during the GA.

Kind regards

Thomas

Bayer: Science For A Better Life

Bayer Pharma Aktiengesellschaft
BPH-DD-ED-TOX-IT, Investigational Toxicology
Berlin: Building S116-5-523
Wuppertal: Building 514-301
Müllerstraße 178, 13353 Berlin, Germany
Tel: +49 30 468 14256
Fax: +49 30 468 18172
Mobil: +49 170 3326034
E-mail: thomas.steger-hartmann@bayer.com
Web: http://www.bayer.com

Vorstand: Dieter Weinand, Vorsitzender | Christoph Bertram
Vorsitzender des Aufsichtsrats: Hartmut Klusik
Sitz der Gesellschaft: Berlin | Amtsgericht Charlottenburg, HRB 283 B